

Appl. No. 10/617,436
 Amdt. Dated December 6, 2004
 Reply to Office action of September 21, 2004

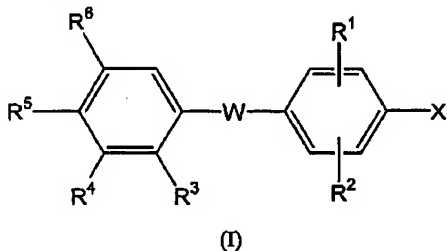
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1 (currently amended): A compound of Formula (I)



the stereoisomers and prodrugs thereof, and the pharmaceutically acceptable salts of said compounds, stereoisomers, and prodrugs, wherein:

W is oxygen, sulfur, $-\text{SO}-$, $-\text{S}(\text{O})_2-$, $-\text{CH}_2-$, $-\text{CF}_2-$, $-\text{CHF}-$, $-\text{C}(\text{O})-$, $-\text{CH}(\text{OH})-$, $-\text{NR}^a$, or $-\text{C}(=\text{CH}_2)-$;

R^1 , R^2 , R^3 , and R^6 are each independently hydrogen, halogen, $-(\text{C}_1-\text{C}_8)\text{alkyl}$, $-\text{CF}_3$, $-\text{OCF}_3$, $-\text{O}(\text{C}_1-\text{C}_8)\text{alkyl}$, or $-\text{CN}$;

R^4 is hydrogen, $-(\text{C}_1-\text{C}_{12})\text{alkyl}$ substituted with zero to three substituents independently selected from Group V, $-(\text{C}_2-\text{C}_{12})\text{alkenyl}$, $-(\text{C}_2-\text{C}_{12})\text{alkynyl}$, halogen, $-\text{CN}$, $-\text{OR}^b$, $-\text{SR}^c$, $-\text{S}(\text{O})\text{R}^c$, $-\text{S}(\text{O})_2\text{R}^c$, aryl, heteroaryl, $-(\text{C}_3-\text{C}_{10})\text{cycloalkyl}$, heterocycloalkyl, $-\text{S}(\text{O})_2\text{NR}^d$, $-\text{C}(\text{O})\text{NR}^d$, $-\text{C}(\text{O})\text{OR}^c$, $-\text{NR}^a\text{C}(\text{O})\text{R}^d$, $-\text{NR}^a\text{C}(\text{O})\text{NR}^d$, $-\text{NR}^a\text{S}(\text{O})_2\text{R}^d$, or $-\text{C}(\text{O})\text{R}^c$; or

R^3 and R^4 are taken together along with the carbon atoms to which they are attached to form a carbocyclic ring of formula $-(\text{CH}_2)_i-$ or a heterocyclic ring of formula $-(\text{CH}_2)_i\text{Q}-(\text{CH}_2)_k-$, wherein Q is oxygen, sulfur, or $-\text{NR}^e$; in which i is 3, 4, 5, or 6; k is 0,

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1, 2, 3, 4, or 5; and 1 is 0, 1, 2, 3, 4, or 5; and wherein said carbocyclic ring and said heterocyclic ring are each substituted with zero to four substituents independently selected from $-(C_1-C_4)alkyl$, $-OR^b$, oxo, $-CN$, phenyl, or $-NR^bR^b$;

R^5 is hydroxy, $-O(C_1-C_6)alkyl$, $-OC(O)R^f$, fluorine, or $-C(O)OR^c$; or

R^4 and R^5 are taken together along with the carbon atoms to which they are attached to form a heterocyclic ring selected from the group consisting of $-CR^a=CR^a-NH-$, $-N=CR^a-NH-$, $-CR^a=CR^a-O-$, $-CR^a=CR^a-S-$, $-CR^a=N-NH-$, and $-CR^a=CR^a-CR^a=N-$;

R^a for each occurrence is independently hydrogen, or $-(C_1-C_6)alkyl$ substituted with zero or one $-(C_3-C_6)cycloalkyl$ or methoxy;

R^b for each occurrence is independently hydrogen, $-(C_1-C_{12})alkyl$ substituted with zero to three substituents independently selected from Group V, aryl, heteroaryl, $-(C_3-C_{10})cycloalkyl$, heterocycloalkyl, $-C(O)NR^dR^d$, or $-C(O)R^f$;

R^c and R^d for each occurrence are each independently hydrogen, $-(C_1-C_{12})alkyl$ substituted with zero to three substituents independently selected from Group VI, $-(C_2-C_{12})alkenyl$, $-(C_2-C_{12})alkynyl$, aryl, heteroaryl, or $-(C_3-C_{10})cycloalkyl$, or heterocycloalkyl;

provided that when R^d is the moiety $-SR^e$, $-S(O)R^e$, or $-S(O)_2R^e$, R^e is other than hydrogen; or

R^e and R^d are taken together along with the atom(s) to which they are attached to form a 3-10 membered heterocyclic ring which may optionally contain a second heterogroup selected from oxygen, NR^e , or sulfur; and wherein said heterocyclic ring is substituted with zero to four substituents independently selected from $-(C_1-C_4)alkyl$, OR^b , oxo, $-CN$, phenyl, or $-NR^bR^b$;

R^e for each occurrence is hydrogen, $-CN$, $-(C_1-C_{10})alkyl$ substituted with zero to three substituents independently selected from Group V, $-(C_2-C_{10})alkenyl$, $-(C_2-C_{10})alkoxy$, $-(C_3-C_{10})cycloalkyl$, aryl, heteroaryl, $-C(O)R^f$, $-C(O)OR^f$, $-C(O)NR^fR^f$, or $-S(O)_2R^f$;

R^f for each occurrence is independently $-(C_1-C_{10})alkyl$ substituted with zero to three substituents independently selected from Group VI, $-(C_2-C_{12})alkenyl$, $-(C_2-C_{10})alkynyl$, $-(C_3-C_{10})cycloalkyl$, or aryl[[.]] heteroaryl, or heterocycloalkyl;

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R^E for each occurrence is independently hydrogen, $-(C_1-C_6)alkyl$, $-(C_2-C_6)alkenyl$, aryl, $-C(O)R^f$, $-C(O)OR^f$, $-C(O)NR^aR^f$, $-S(O)_2R^f$, or $-(C_3-C_8)cycloalkyl$;

Group V is halogen, $-CF_3$, $-OCF_3$, $-OH$, oxo, $-(C_1-C_6)alkoxy$, $-CN$, aryl, heteroaryl, $-(C_3-C_{10})cycloalkyl$, heterocycloalkyl, $-SR^f$, $-S(O)R^f$, $-S(O)_2R^f$, $-S(O)_2NR^aR^f$, $-NR^bR^E$, or $-C(O)NR^aR^f$;

Group VI is halogen, hydroxy, oxo, $-(C_1-C_6)alkoxy$, aryl, heteroaryl, $-(C_3-C_8)cycloalkyl$, heterocycloalkyl, $-CN$, or $-OCF_3$;

provided that when R^f is $-(C_1-C_{12})alkyl$ substituted with zero to three substituents independently selected from Group V, wherein said Group V substituent is oxo, said oxo group is substituted on a carbon atom other than the C_1 carbon atom in $-(C_1-C_{12})alkyl$;

aryl for each occurrence is independently phenyl or naphthyl substituted with zero to four substituents independently selected from halogen, $-(C_1-C_6)alkyl$, $-CN$, $-SR^f$, $-S(O)R^f$, $-S(O)_2R^f$, $-(C_3-C_6)cycloalkyl$, $-S(O)_2NR^aR^f$, $-NR^bR^E$, $-C(O)NR^aR^f$, $-OR^b$, perfluoro- $-(C_1-C_4)alkyl$, or $-COOR^f$;

provided that when said substituent(s) on aryl are $-SR^f$, $-S(O)R^f$, $-S(O)_2R^f$, $-S(O)_2NR^aR^f$, $-NR^bR^E$, $-C(O)NR^aR^f$, $-OR^b$, or $-COOR^f$, said substituents R^b , R^f , and R^E are other than aryl or heteroaryl;

heteroaryl for each occurrence is independently a 5, 6, 7, 8, or 9-membered monocyclic or bicyclic ring having from one to three heteroatoms selected from O, N, or S;

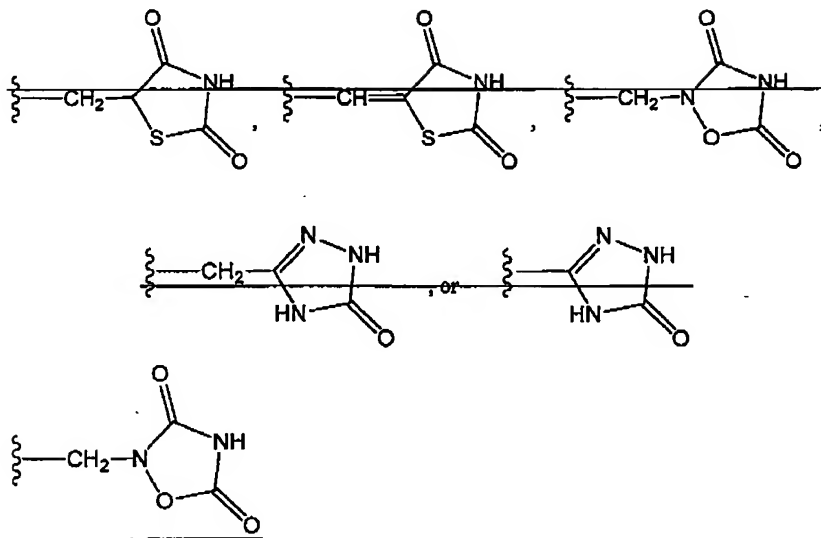
wherein in said bicyclic ring, a monocyclic heteroaryl ring is fused to a benzene ring or to another heteroaryl ring, and having zero to three substituents independently selected from halogen, $-(C_1-C_4)alkyl$, $-CF_3$, $-OR^b$, $-NR^aR^E$, or $-COOR^f$;

provided that when said substituent(s) on heteroaryl are $-NR^aR^E$, $-OR^b$, or $-COOR^f$, said substituents R^b , R^f , and R^E are other than aryl or heteroaryl;

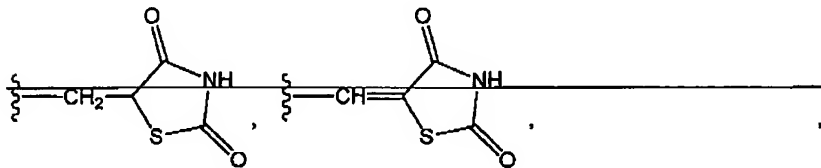
heterocycloalkyl for each occurrence is independently a 5, 6, 7, 8, or 9-membered monocyclic or bicyclic cycloalkyl ring having from one to three heteroatoms selected from oxygen, $-NR^a$, or sulfur, and having zero to four substituents independently selected from $-(C_1-C_4)alkyl$, $-OR^b$, oxo, $-CN$, phenyl, or $-NR^aR^E$; and

X is

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with the proviso that when W is oxygen, sulfur, SO, or SO₂, then X is not represented by



Claim 2(original): A compound according to claim 1 wherein W is oxygen.

Claim 3(currently amended): A compound according to claim 1 wherein:

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R^1 is located at the 3-position and R^2 is located at the 5-position, wherein R^1 and R^2 are each independently hydrogen, $-(C_1-C_6)$ alkyl, halogen, or $-CN$;

R^3 is hydrogen, $-(C_1-C_4)$ alkyl or halogen;

R^4 is $-(C_1-C_{10})$ alkyl substituted with zero to three substituents independently selected from fluoro, hydroxy, oxo, aryl, heteroaryl, or $-(C_3-C_8)$ cycloalkyl, or heterocycloalkyl, $-S(O)_2NR^aR^d$, $-C(O)NR^aR^d$, $-S(O)_2R^c$, $-(C_3-C_8)$ cycloalkyl, heterocycloalkyl, $-C(O)R^c$, $-OR^b$, $-SR^c$, $-S(O)R^c$, $-NR^aC(O)R^d$, $-NR^aC(O)NR^cR^d$, or $-NR^aS(O)_2R^d$; or

R^a and R^d are taken together along with the atom(s) to which they are attached to form a 3-10 membered heterocyclic ring which may optionally contain a second heterogroup selected from oxygen, NR^e , or sulfur, and wherein the heterocyclic ring is substituted with zero to four substituents independently selected from $-(C_1-C_4)$ alkyl, OR^b , oxo, $-CN$, phenyl, or $-NR^eR^f$; or

R^3 and R^4 are taken together along with the carbon atoms to which they are attached to form a carbocyclic ring of formula $-(CH_2)_i-$ or a heterocyclic ring of formula $-(CH_2)_k-Q-(CH_2)_l-$ wherein Q is O , S , or NR^e ; in which i is 3, 4, 5 or 6; k is 0, 1, 2, 3, 4 or 5; and l is 0, 1, 2, 3, 4 or 5; and wherein said carbocyclic ring and said heterocyclic ring are each substituted with zero to four substituents independently selected from $-(C_1-C_4)$ alkyl, $-OR^b$, oxo, $-CN$, phenyl, or $-NR^eR^f$;

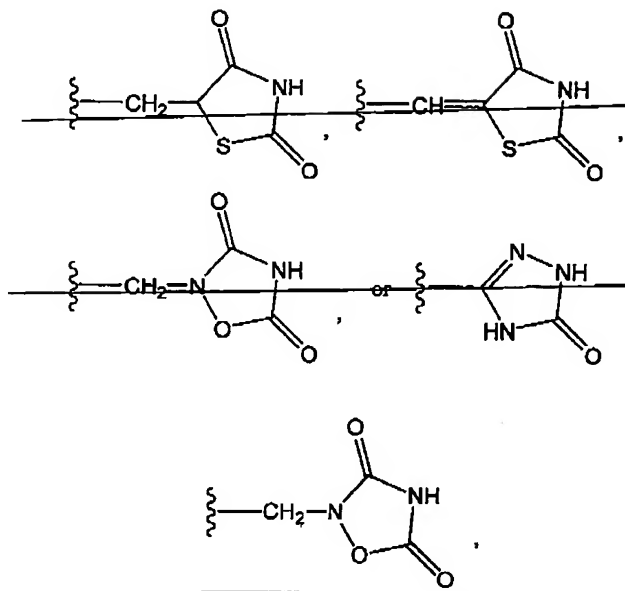
provided that when R^4 is $-(C_1-C_{10})$ alkyl substituted with zero to three substituents, said oxo group is substituted on a carbon atom other than the C_1 carbon atom in $-(C_1-C_{10})$ alkyl;

R^5 is $-OH$, $-OC(O)R^f$, $-C(O)OR^c$, or $-F$; wherein R^f is $-(C_1-C_{10})$ alkyl substituted with zero to three substituents independently selected from Group VI;

R^6 is hydrogen, halogen or $-(C_1-C_4)$ alkyl; and

X is

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Claim 4(currently amended): A compound according to claim 3 wherein

R^1 and R^2 are each independently hydrogen, $-(C_1-C_6)alkyl$, halogen, or $-CN$;

R^3 is hydrogen;

R^4 is $-(C_1-C_{10})alkyl$ substituted with zero to three substituents independently selected from fluoro, hydroxy, oxo, aryl, heteroaryl, or $-(C_3-C_8)cycloalkyl$, or heterocycloalkyl, $-S(O)_2NR^cR^d$, $-C(O)NR^cR^d$, $-S(O)_2R^c$, $-(C_3-C_8)cycloalkyl$, heterocycloalkyl, $-C(O)R^c$, $-OR^b$, $-SR^c$, $-S(O)R^c$, $-NR^aC(O)R^d$, $-NR^aC(O)NR^cR^d$, or $-NR^aS(O)_2R^d$; or

R^2 and R^d are taken together along with the atom(s) to which they are attached to form a 3-10 membered heterocyclic ring which may optionally contain a second heterogroup selected from oxygen, $-NR^e$, or sulfur; and wherein the heterocyclic ring is substituted with zero to four substituents independently selected from $-(C_1-C_4)alkyl$, $-OR^b$, $-exo$, $-CN$, $-phenyl$, or $-NR^aR^e$;

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R^5 is -OH, fluoro, or -OC(O) R^f wherein R^f is -(C₁-C₁₀)alkyl substituted with zero to three substituents independently selected from Group VI; and

R^6 is hydrogen.

Claim 5(currently amended): A compound according to claim 4 wherein

R^1 and R^2 are both methyl, bromo, or chloro;

R^4 is -(C₁-C₁₀)alkyl, substituted with zero to two substituents independently selected from fluoro, hydroxy, oxo, aryl, ~~heteroaryl~~, or -(C₃-C₈)cycloalkyl, ~~or heterocycloalkyl~~, -S(O)₂NR^aR^d, -C(O)NR^aR^d, -S(O)₂R^c, -(C₃-C₈)cycloalkyl, ~~heterocycloalkyl~~, -C(O)R^c, -OR^b, -SR^a, -S(O)R^c, -NR^aC(O)R^d, -NR^aC(O)NR^cR^d, or -NR^aS(O)₂R^d; ~~or~~

~~R^b and R^d are taken together along with the atom(s) to which they are attached to form a 3-10 membered heterocyclic ring which may optionally contain a second heterogroup selected from oxygen, NR^a, or sulfur, and wherein the heterocyclic ring is substituted with zero to four substituents independently selected from (C₁-C₄)alkyl, OR^b, oxo, -CN, phenyl, or -NR^aR^e; and~~

R^5 is -OH.

Claim 6(currently amended): A compound selected from the group consisting of:

2-[3,5-dichloro-4-(4-hydroxy-3-isopropyl-phenoxy)-benzyl]-

[1,2,4]oxadiazolidine-3,5-dione;

2-[4-(3-isopropyl-4-methoxy-phenoxy)-3,5-dimethyl-benzyl]-

[1,2,4]oxadiazolidine-3,5-dione; ~~and;~~

2-[4-(4-hydroxy-3-isopropyl-phenoxy)-3,5-dimethyl-benzyl]-

[1,2,4]oxadiazolidine-3,5-dione; ~~and~~

~~5-[4-(4-hydroxy-3-isopropyl-phenoxy)-3,5-dimethyl-phenyl]-2,4-dihydro-[1,2,4]triazol-3-one~~, the stereoisomers and prodrugs thereof, and the pharmaceutically acceptable salts of said compounds, stereoisomers, and prodrugs.

Claims 7-17(previously cancelled)

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Claim18 (original): A pharmaceutical composition comprising a compound of Formula (I), a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer or prodrug, as defined in claim 1.

Claims 19-25 (previously cancelled)

Claims 26 and 27 (cancelled)